Remarks

The Office Action of October 2, 2006, has been received and reviewed. Claims 1-4, 6, 8-10, 12, 15-23, 25-30, 32, 33, 35-37, 39, 42 and 43 are currently pending in the application. Claims 12, 15-23, 35, 36, 32, 33, 35-37, 39, 42 and 43 are withdrawn from consideration as being directed to a non-elected invention. Claims 1-4, 6, 8-10, and 27-30 stand rejected. Claims 1 and 27 are amended herein. New claims 44 and 45 are added and find support in the as-filed specification including, at least, claims 1 and 27. All amendments and cancellations are made without prejudice or disclaimer. Reconsideration is respectfully requested. Submitted herewith is a Petition for Extension of Time under 37 C.F.R. § 1.136(a) for a three (3) month extension.

Claim Objection

Claims 1 and 27 are objected to because the claims refer to "consisting of parts spanning from amino acid residue 25-442, 97-318, 97-442 and 97-545 . . . as depicted in FIG. 1." It was asserted that the number of residues in FIG. 1 can only refer to nucleotide residues, not amino acid residues. (Office Action, page 2). Applicants respectfully traverse the rejection.

Claims 1 and 27 refer to nucleic acids encoding functional parts of an AMA-1 ectodomain, the nucleic acids being specified by the amino acid number in the protein. The reference protein is the protein as depicted in FIG.1. The numbering in the figure is a nucleotide numbering, but claims 1 and 27 refer to an amino acid numbering. The claim has been amended to further clarify this distinction. Reconsideration and withdrawal of the objection is requested.

35 U.S.C. §112, first paragraph

Claims 1-4, 6, 8-10 and 27-30 stand rejected under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the written description requirement. The claims allegedly contain subject matter which was not described in the specification in such as way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Applicants respectfully traverse the rejection.

The rejection was directed to the language in the independent claims wherein the encoding nucleic acid "consists" of a sequence as depicted in FIG. 1. It was asserted that the specification did not contemplate the element "consists of." Applicants respectfully disagree.

While not conceding this point, applicants have deleted the element from independent claims 1 and 27. Reconsideration and withdrawal of the rejection is requested.

Claims 1-4, 6, 8-10 and 27-30 stand further rejected for claims to portion of the sequence of FIG. 1 and all sequences with a least 90% homology to said portions. Applicants respectfully disagree. While not conceding this point, applicants have deleted the element from independent claims 1 and 27. As such, applicants respectfully submit that claims 1 and 27 fulfill the written description requirement. Further, applicants assert that claims 2-4, 6, 8-10, and 28-30 are allowable at least as depending, directly or indirectly, from independent claims 1 and 27. As such, reconsideration and withdrawal of the rejection under 35 U.S.C. § 112, first paragraph, is respectfully requested.

Rejection Under 35 U.S.C. § 102(b)

Claims 1-4, 6, 8-10 and 27-30 stand rejected under 35 U.S.C. § 102(b) as assertedly being anticipated by Kocken *et al.* Applicants respectfully traverse the rejection.

"Kocken *et al.* teach the expression of *P. vivax* AMA-1." (February 10, 2006, Office Action, page 8). Kocken cannot describe "a method for producing mRNA encoding a *Plasmodium falciparum* apical membrane antigen-1 (AMA-1) ectodomain, or a functional part thereof, in a yeast cell, said method comprising: providing said yeast cell with a nucleic acid encoding said (*Plasmodium falciparum* AMA-1) ectodomain or functional part thereof" or "wherein the encoding nucleic acid comprises a nucleotide sequence of FIG. 1 encoding the ectodomain or the functional part thereof" as Kocken fails to describe, either expressly or inherently, a *Plasmodium falciparum* sequence or the sequence depicted in FIG. 1. Therefore, Kocken *et al.* cannot anticipate the claims 1 and 27.

Furthermore, applicants respectfully assert that claims 2-3, 6, 9-10, and 28-30 are allowable at least as depending, directly or indirectly, from independent claims 1 and 27. As such, reconsideration and withdrawal of the rejection of claims 1-3, 6, 9-10, and 27-30 under 35 U.S.C. § 102(b) are respectfully requested.

Rejection under 35 U.S.C. § 103(a)

Claims 1-3, 5-6, 9-10, 27-30 and 45 stand rejected under 35 U.S.C. § 103(a) as assertedly being obvious over Kocken *et al.* in view of Withers-Martinez. Claim 45 has been canceled, thus the rejection is moot as to this claim. Claim 5 was previously canceled. Applicants respectfully traverse the rejection.

As stated herein, Kocken fails to teach or suggest expression of the *P. falciparum* AMA-1 ectodomain or a functional part thereof as recited in independent claims 1 and 27. Kocken also fails to teach or suggest "wherein at least one glycoslyation site is removed from said *Plasmodium falciparum* AMA-1 ectodomain." Withers-Martinez fails to cure the deficiencies of Kocken. Withers-Martinez is focused on the *pfsub*-1 gene, not the *Plasmodium falciparum* AMA-1 ectodomain. The specific *pfsub*-1 gene cannot be extrapolated to every *Plasmodium falciparum* gene. The claims are directed toward a specific nucleic acid sequence and specific fragments thereof. As described in the Noonan reference provided herewith, the MDRI protein was expressed using various nucleic acids that, albeit encoding the same amino acid, used different codons to do so. Noonan observed differences in the function of the MDRI protein which is contrary to conventional thought that protein function is determined by the amino acid sequence of the protein.

Withers-Martinez teaches two methods for production of their protein. A first method involves *P. pastoris* and a second method involves insect cells. It was asserted that Withers-Martinez describes the AMA-1 ectodomain in native conformation or at least a portion thereof obtained from the yeast cells. Withers-Martinez does not teach or suggest AMA-1 protein or *pfsub*-1 protein in the native conformation produced by the *Pichia* cells. Withers-Martinez specifically states that the protein produced by the *Pichia* cells accumulates in insoluble form in the yeast cells. (Withers-Martinez, page 1118, middle of the left column). Withers-Martinez lacks any disclosure that any of this protein is naturally folded.

The *pfsub*-1 protein produced in Withers-Martinez is produced using tunicamycin (*Id.*, page 1115, middle of both columns). Tunicamycin is used to at least partially inhibit glycosylation of proteins. Thus, the *pfsub*-1 protein contains glycosylation sites, whereas the protein produced in the present invention does not. In addition, assuming the insoluble *Pichia* produced *pfsub*-1 protein includes naturally folded protein (which applicants do not concede),

this protein also differs from the present claims. The tunicamycin treatment does not prevent glycosylation completely. The claims are directed toward a protein "wherein at least one glycoslyation site is removed from said *Plasmodium falciparum* AMA-1 ectodomain." Thus, the product produced in the present invention differs from the protein produced by Withers-Martinez with respect to glycosylation.

Protein expression is an empirical science. Thus, no general teaching may be derived from combining the teaching of Kocken and Withers-Martinez. Applicant has empirically determined that some fragments cannot be expressed in *Pichia* cells despite the use of synthetic codon optimizing gene. An example of such a fragment is a prosequence-Domain I fragment of AMA-1 ectodomain (unpublished data).

As the combination of Kocken in view of Withers-Martinez fails to teach or suggest every element of the presently claimed invention, independent claims 1 and 27 are not rendered obvious by the proposed combination of art. Reconsideration and withdrawal of the rejection is requested.

Furthermore, claims 2-4, 6, 8-10, and 28-30 are allowable at least as depending, directly or indirectly, from independent claims 1 and 27. As such, reconsideration and withdrawal of the rejection of claims 1-4, 6, 8-10, and 27-30 under 35 U.S.C. § 103(a) are respectfully requested.

Conclusion

In view of the foregoing amendments and remarks, Applicants submit that the claims define patentable subject matter and a notice of allowance is requested. Should questions exist after consideration of the foregoing, the Office is kindly requested to contact the Applicants' attorney at the address or telephone number given herein.

Respectfully submitted,

Krista Weber Powell
Registration No. 47,867
Attorney for Applicants
TRASKBRITT
P.O. Box 2550
Salt Lake City, Utah 84110-2550
Telephone: 801-532-1922

Date: [redacted]
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